

REMARKS**Status of the Claims**

Claims 7, 11, 12, 14, 19, 22, 23, 36, 37, 41, 42, 46-48, 51, 53, 54, 59, 66, 69, 70, 72-90, 91-94, 112, 113, 114, 115 and 117-132 are pending in the present application. Support for the amendments to the claims includes, but is not limited to, the description in claims 17 and 53 as well as the description on page 17, lines 25-26 of the specification. Claim 131 further limits the amount of active ingredient. The composition according to claim 132 is supported, for instance, at page 11, last paragraph - page 12, first paragraph. Claims 30 and 53 have been cancelled so that the number of claims remains unchanged.

This amendment places the application into immediate condition for allowance or places the claims in better form for appeal. No new issues are introduced by this claim amendment.

Claim Rejections - 35 U.S.C. §103

The Examiner has rejected claims 7, 11, 12, 14, 19, 22, 23, 36, 37, 41, 42, 46-48, 51, 53, 54, 59, 66, 69, 70, 72-90, 91-94, 112, 113, 114, 115 and 117-128 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 4,736,024 to Della Valle et al. in view of U.S. Patent No. 4,141,973 to Balazs. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

The Present Invention

Each of the present independent claims have been amended to recite claimed amount(s) of ingredients that clearly distinguish over the cited prior art. Further, the claimed noncarrier

ingredients are either at least one glycosaminoglycan or, for instance, HA.

Further, the Examiner has not commented on the patentability of either claims 53 or 93. The Examiner is required to examine all of the claims and not just selected claims.

Based upon a review of the cited prior art and based upon the knowledge in the art, it is clear that there is no motivation to use the claimed amounts of active ingredients without destroying the teachings of the prior art cited by the Examiner. Accordingly, the Examiner clearly has not set forth a prima facie case of obviousness.

In order to further support Applicants' position, the Examiner is invited to review the teachings of the Della Valle patent very closely. In this regard, the Examiner mentions that Della Valle specifically talks about formulations containing from 34% to 80% HA. The concentrations of HA in the claimed invention are well below this level. In fact, in all of the formulations and EXAMPLES that Della Valle describes, the HA is well above 50% of the final formulation. See column 9, line 36 through all of the examples wherein the HA is a significant proportion of the formulation. This is typical for carriers. One skilled in the art would never add that high a concentration of the active ingredient.

More specifically, Formulation 11 of Della Valle contains a total of 100g of which HA makes up 85% wt/wt (85 grams in 100 grams).

Formulation 2 contains a total of 100g of which HA makes up 100g and the active ingredient is 2 grams.

Formulation 3 contains a total of 100g of which HA makes up 98.5 g or 98.5%.

Formulation 4 refers to EXAMPLE 18 which describes 98.5 g of HA with 2.34g of pilocarpine.

Formulation 5 refers to EXAMPLE 16 which describes 4g of HA in a total yield of 7.35g or HA is 54.4%.

Formulation 6 refers to EXAMPLE 17 which describes an HA content of 82.8%.

Formulation 7 refers to EXAMPLE 15 which describes an HA content of 73%.

Moreover, all of the Della Valle EXAMPLES contain HA concentrations as follows:

EXAMPLE 1 -- HA = 66.2%

EXAMPLE 2 -- HA = 34%

EXAMPLE 3 -- HA = 75.8%

EXAMPLE 4 -- HA = 78.8%

EXAMPLE 5 -- HA = 80%

EXAMPLE 6 -- HA = 72.3%

EXAMPLE 7 -- HA = 41.8%

EXAMPLE 8 -- HA = 61.3%

EXAMPLE 9 -- HA = 40%

EXAMPLE 10 -- HA = 64.3%

EXAMPLE 11 -- HA = 69.4%

EXAMPLE 12 -- HA = 56.7%

EXAMPLE 13 -- HA = 64.6%

EXAMPLE 14 -- HA = $4\text{g}/4.85\text{g} = 82.4\%$

EXAMPLE 15 -- HA = 73%

EXAMPLE 16 -- HA = 83%

EXAMPLE 17 -- HA = 82.8%

EXAMPLE 18 -- HA = $98.31\text{g}/99.8\text{g} = 98.5\%$

EXAMPLE 19 -- HA = $98.68\text{g}/99.8\text{g} = 99.2\%$

EXAMPLES 20 to 25 describe methods of manufacturing HA and have nothing to do with the concentration of HA in a formulation.

EXAMPLE 26 -- HA = 66.2%

EXAMPLE 27 -- HA = 64.3%

EXAMPLE 28 -- HA = $4.47\text{g}/4.5\text{g} = 99.3\%$

EXAMPLE 29 -- HA = 69.4%

EXAMPLE 30 -- HA = $7.15\text{g}/7.35\text{g} = 97.3\%$

Clearly, the prior art teaches away from the claimed amount of active ingredient. Modifying the prior art in order to obtain the present invention would destroy the teachings thereof and such hindsight reconstruction of the prior art in an attempt to obtain the present invention is not acceptable under US practice.

The Examiner seems to indicate that it would be obvious to substitute pure HA for impure HA and vice versa. Such a position is without technical basis as one of ordinary skill readily knows that these materials are not functionally equivalent. Indeed, any one of ordinary skill in the art would immediately know that they can not utilize impure materials for surgery or for use within the body, for example, by injection. Substituting impure materials for pure materials would cause adverse reactions and render the prior art unfit for its intended purpose. Modifying the prior art in the manner suggested by the Examiner to obtain the invention destroys the teachings thereof. In re Gordon, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984). Also see MPEP 2143.01, page 2100-140 Rev, 6, 2007.

Further, using the Examiner's logic, it appears that the carrier of the prior art corresponds to the claimed active ingredient. [However, the activity of the claimed active ingredient is discussed in the specification, contrary to the Examiner's position. See page 7, last paragraph, page 8, second paragraph, page 8, line 31- page 9, line 4, page 11, lines 5-10 and 16-22, page 11, line 31 – page 17.] Assuming the Examiner's position is that the prior art carrier corresponds to the claimed active ingredient, then there is no rational basis for modifying the prior art carrier to be present in the amount of the claimed active ingredient.

Further, claim 132 recites that the "at least one glycosaminoglycan is present as the sole active ingredient," thereby excluding the active ingredient of the cited prior art. In the context of

the present invention, the claimed composition of claim 132 excludes any other active ingredient that is not a glycosaminoglycan(s).

Moreover, the claimed carrier clearly excludes HA since the claimed active ingredient is either glycosaminoglycan or HA and the present specification and claims clearly require separate active ingredients and carriers. What component of the cited prior art corresponds to the claimed carrier? The Examiner seems to indicate that the cited prior art carrier is the claimed active ingredient. There is no suggestion that the prior art active ingredient should be excluded so that only carriers should be administered.

The present inventors utilize “carrier” in the conventional sense such that the “carrier” is not active. Such a conventional definition excludes active carriers such as HA. That is, the present inventors do not assign a nonconventional definition to the term “carrier.”

Further, the type of carrier required by claims 19, 22, 23, 70, 73, 92, 94, 112, 117, 119, 128, 129 and 130 also excludes HA as the carrier. For instance, in many of these claims, the carrier is a drink, a drink mix, a food, a candy, a mouthwash, a toothpaste, a gargle, a vaporizer liquid, a gum, a lozenge, an ingestible gel, an ingestible foam, an ingestible capsule, a tablet, an ingestible tablet, an ingestible dissolvable tablet, a suppository, and an ingestible nutritional supplement.

So, is the Examiner’s position that one of ordinary skill in the art would modify the amount of the prior art carrier, which allegedly corresponds to the claimed active ingredient, to be present in such a small amount that it can not be used to carry the active ingredient of the prior art reference? Clearly, such a position is hindsight and without rational basis.

In addition, one of ordinary skill in the art would readily know that pure and impure HA

are not interchangeable. See the Examiner's comments on page 4, second paragraph of the office action. There is no technical basis to support the Examiner's conclusion and there can be no prima facie case of obviousness established utilizing such a rationale. Is it the Examiner's position that impure substances can be injected into the eye or used for surgery? Also see page 6, first paragraph of the Office Action.

Balasz is directed to highly pure HA and any one of ordinary skill in the art knows that impure substances such as food quality materials are not injected into the body. Balasz excludes impure HA. The title, the abstract, the claims and virtually the entire specification teach that pure HA is not equivalent to impure HA.

U.S. Patent No. 4,736,024 to Della Valle et al. [Della Valle] recites pharmaceutical preparations for topical administration containing a pharmacologically active substance together with HA. Clearly, HA is not the active ingredient in the Della Valle compositions. Rather, Della Valle expressly teaches that HA is the vehicle or carrier to be used with "one or more pharmacologically active substances." See, for instance, abstract and col. 1, lines 11-25.

Indeed, HA is never intended to be used as an active ingredient in Della Valle. See col. 5, lines 55-60. Moreover, HA is specifically defined as the vehicle or carrier in Della Valle. Clearly, HA is only desirable as a carrier in Della Valle. Obviously, one of ordinary skill in the art would recognize that the definition of vehicle in Della Valle is unique to Della Valle since vehicles/carriers in the art are generally known to be inert/not active.

The desirable properties of HA as a carrier are set forth, for instance, in col. 2, lines 44-51 and 65 - col. 3, line 9 of Della Valle. Clearly, HA is intentionally not included in the definition of an active ingredient in Della Valle. As the Examiner points out, Della Valle knew

that ultrapure HA [eg. of Balazs] was active. However, Della Valle intended HA's use as a carrier for other active ingredients. This point is further emphasized in the definitions of "Component (1) -Pharmaceutical Substance," which begins at col. 3, line 16. In fact, HA is clearly limited to use as "Component (2) – Hyaluronic Acid Vehicle" beginning at col. 5, line 14. Della Valle then combines these mutually exclusive components beginning at col. 7, line 30. Also see the Della Valle examples.

Accordingly, Della Valle **EXPRESSLY** teaches away from the use of HA as an active ingredient as claimed in the present invention. Notwithstanding this express teaching, the Examiner says that because HA inherently has activity, it would be obvious to use it as the active ingredient together with the active ingredient of Della Valle. That is, it would be obvious to modify the Della Valle composition by ignoring the purpose of the Della Valle composition and modifying it to obtain the claimed composition.

Balazs teaches **ultrapure HA** and the use thereof. In Balazs, the ultrapure HA is the active ingredient. However, even in Balazs, the activity refers to replacement of the the fluid in the eye, not a pharmacological activity that produces a functional result such as relief of pain, swelling and itching.

The Examiner relies upon the teachings at col. 5, lines 15-45, which recites Balazs, in order to provide motivation for combining the teachings of Della Valle and Balazs. But, the Examiner ignores the description which immediately follows, for instance, at col. 5, lines 56 – 60 of Della Valle, which states:

In contrast to this therapeutic use...in the present invention, hyaluronic acid or its molecular fractions are used as **vehicles** for administration of pharmacologically active substances for topical use.

The Examiner's reliance upon only a portion of the teachings of Della Valle with respect to Balazs clearly ignores the express "teaching away" by Della Valle. Contrary to the Examiner's position, there can be no motivation to combine the teachings of Della Valle in the manner suggested. This is especially true since modifying the teachings of Della Valle in order to obtain the present invention is directly contrary to and destroys the teachings of Della Valle.

Accordingly, one of ordinary skill in the art upon reading the teachings of the Della Valle and Balazs – e.g. as contemplated by Della Valle – would not obtain the present invention. The Examiner's position is directly contrary to the teachings of Della Valle, since Della Valle states that in contrast to col. 5, lines 15-45 [relied on by the Examiner for motivation], one of ordinary skill in the art MUST go in a DIFFERENT direction. That is, HA should be used as a vehicle [carrier] and not as an active ingredient in his invention. Since Della Valle was aware of Balazs and teaches the opposite of what the Examiner suggests, there is no motivation for combining these references in the manner suggested and the rejection should be withdrawn.

Further, the Examiner concedes that the types of the claimed carriers are not disclosed in either Della Valle and Balazs. See last paragraph on page 6 of Office Action. The Examiner ignores that Balazs uses ultrapure for HA surgical uses. Certainly, such surgical uses of highly pure and very expensive material can not suggest the claimed formulations including carriers such as a drink, a drink mix, a food, a candy, a mouthwash, a toothpaste, a gargle, a vaporizer liquid, a gum, a lozenge, an ingestible gel, an ingestible foam, an ingestible capsule, a tablet, an ingestible tablet, an ingestible dissolvable tablet, a suppository, and an ingestible nutritional supplement. Such a combination would not even cross the mind of one of ordinary skill due to

cost reasons alone. The same logic applies to Della Valle.

In the first paragraph on page 4 of the Office Action, the Examiner states that “since the HA can be applied orally or nasally it would have been obvious to someone skilled in the art that HA is of at least food grade purity.” Such a conclusion is without basis. One of ordinary skill in the art would immediately know that food grade purity HA is so impure that it would NEVER be used for surgery and it would NEVER pass the test required by the cited prior art e.g. monkey eye test. Therefore, even if the references were combined in the manner suggested by the Examiner, the combination would not suggest the present invention since the present invention allows for impure HA [eg food or cosmetic grade] whereas Balazs clearly does not allow for such impure materials. Thus, the combination would not suggest the present invention e.g. see claims 23, 72, 73, 92, 94, wherein a suitable active ingredient must pass the claimed purity test to be within the scope of the invention, or claim 59, wherein a suitable active ingredient is non pure or low purity or food grade.

In summary, in the present invention, it is the glycosaminoglycan/hyaluronic acid in the claimed amount, which is orally or mucosally administered as an active ingredient, that produces a pharmacological effect. In contrast, in Della Valle, it is the non-HA active ingredient and not the vehicle [HA] which is to produce the desired pharmacological effect. There is no motivation to delete the active ingredient of Della Valle so as to merely use the vehicle as the active ingredient. Such a conclusion is directly contrary to Della Valle. Also, there is no technical basis to use the Balazs ultrapure HA as an active ingredient in Della Valle since Della Valle was aware of Balazs and expressly decided not to use the ultrapure HA of Balazs as the active ingredient. On the contrary, Della Valle decided to use pure HA as a carrier together with other active

ingredients. Such a composition does not suggest the claimed composition.

Moreover, there is no suggestion to utilize non pure HA such as food grade HA in either reference. One of ordinary skill would never use low grade HA for surgery due to the impurities. Such a modification would destroy the teachings of the underlying references. Accordingly, the rejection should be withdrawn since the combination does not suggest the present invention.

Finally, rejoinder of the method claims is requested.

If the present amendment does not place the application into condition for allowance, then the Examiner is requested to contact the undersigned at 703-205-8000.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Marc S. Weiner, Reg. No. 32,181 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

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Respectfully submitted,

By 

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